The concept of the study was imaginative, but it should have been continued for longer and/or recruited more couples. Behaviour modification to avoid HIV transmission risks remains the only method we have for combating AIDS, and it is too important to be predicated on unsound "nil risk" conclusions.

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What is soluble?

SIR— "Science, as famously defined by Sir Peter Medawar, is the art of the soluble" writes a *Lancet* book reviewer (July 23, p 250). Medawar answered Arthur Koestler's question (in *The Act of Creation*)—why did scientists not engage in "intense research" on "the genetics of behaviour?"—by pointing out that "the problem is very, very difficult" and is unlikely to yield to "direct assault". He went on, "No scientist is admired for failing in the attempt to solve problems that lie beyond his competence . . . If politics is the art of the possible, research is surely the art of the soluble. Both are immensely practical-minded affairs" (*The Art of the Soluble*, 1967, p 87). I doubt if Medawar would have thought his epigram improved by the substitution of "Science" for "research". The epigram on politics that inspired Medawar came from the German Chancellor, Bismarck in 1867.

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Sex differences in measles fatality and Edmonston-Zagreb measles vaccine

SIR—Dilraj and Karim (May 28, p 1366) indicate that use of high-titre Edmonston-Zagreb (EZ) vaccine at 6 months of age coincided with a significantly higher case-fatality ratio for girls with measles admitted to the measles wards at Clairwood Hospital, Durban, South Africa, than for boys. However, it seems unlikely that an increase in risk of death from measles in girls who received high-titre EZ vaccine was responsible for the sex-specific difference observed.

The case-fatality ratio for girls was very similar during the 2 years before the "EZ period" and the 20-month EZ period (4·4% *vs* 5·4%; not significant) whereas the case-fatality ratio for boys fell significantly (4·7% *vs* 1·7%; p=0·006). Thus, a significant reduction in the case-fatality ratio for boys with measles during the EZ period was mainly responsible for the sex differences, not an increase in case-fatality among girls.

The case-fatality ratio for girls fell between the EZ period and the post-EZ interval of September to December, 1992, (5·4% to 1·2%, p=0·024). Although the age at death of measles cases was not given, it will have substantially exceeded the age at immunisation for those who were immunised. Thus the reduced case-fatalities for boys (1·6%) and girls (1·2%) in this post-EZ interval would have reflected, in part or perhaps even primarily, the mortality experience of children eligible to receive high-titre vaccine during the preceding 20-month EZ period.

5 of 8 patients admitted during the EZ period who had documentation of immunisation status had not been vaccinated. If this proportion is representative of all admissions during the EZ period, differences in sex-specific mortality ratios would have been determined mainly by the mortality experience in unvaccinated rather than vaccinated children.

In our Senegal studies,[1] we observed high and comparable vaccine efficacy on exposure to measles cases for several years after high-titre EZ at 5 months (92%) and Schwarz standard vaccine at 10 months (97%). Furthermore, we have observed no acute-phase measles deaths in the few measles cases that have occurred in Senegalese children vaccinated with high-titre EZ. Measles case-fatality ratios in Senegalese children previously vaccinated with any vaccine are significantly reduced (unpublished). Similar observations on EZ and Schwarz vaccines have been made in Guinea-Bissau.[2]

Coverage rates in the Natal KwaZulu region were not reported but coverage with measles vaccine probably increased during this time period due to an accelerated vaccination campaign,[3] and the reductions in annual numbers of measles cases admitted to Clairwood Hospital suggest that this campaign was effective. As coverage increases so the proportion of measles cases previously vaccinated rises, even though efficacy remains high. An increase in the proportion of measles cases who were previously vaccinated may underlie the lower case-fatality ratios seen in girls and boys in the post-EZ period.

A reanalysis of community data from Machakos, Kenya, shows that measles case-fatality ratios declined simultaneously with improved immunisation coverage with standard doses of Schwarz vaccine at 8–9 months.[4] The decline in case-fatality ratio was more rapid for boys, leading to significantly higher case-fatality ratio for girls despite a general decline in the severity of measles. Hence in the initial phase, boys in Machakos may have benefited more. We do not know whether these similar trends in case-fatality ratios, for different vaccines in different sites, were caused by the same factors.

Available data on mortality in children admitted to the measles wards at Clairwood do not permit an inference that high-titre EZ was ineffective in preventing measles or that it was responsible for the sex-specific changes in case-fatality ratios.

We doubt if the sex-specific changes in measles case-fatality ratios are related in any way to our observations of a higher incidence of non-measles deaths in girls receiving high-titre Schwarz and EZ vaccines at 5 months compared with girls given standard doses of Schwarz vaccine at 10 months.

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